BRITISH PHARMACOPOEIA COMMISSION

Expert Advisory Group: Antibiotics

SUMMARY MINUTES

A meeting of Expert Advisory Group: Antibiotics was held at 10 South Colonnade, Canary Wharf, London E14 4PU on Thursday 27th September 2018.

Present: Dr R Horder *(Chair),* Dr G Cook (*Vice-chair*), Mr G Blake, Mr E Flahive, Dr W Mann, Prof J Miller, Dr M Pires and Mr I Williams. Mr J Sumal attended the meeting for the item discussed under minute 434.

Apologies: V. Jaitely.

In attendance: Mr S Maddocks, Mr A Evans, Ms K Busuttil and Ms M Nanasi. Mr. M Whaley attended the meeting for the item discussed under minute 431.

414 **Introductory remarks**

Welcome
The Chair welcomed members to the meeting. A special welcome and thanks was extended to Ms Busuttil and Ms Nanasi from the BP Laboratory.

Declaration of Interests
Members were reminded to declare specific interests as they arose during the meeting and to inform the secretariat of any changes throughout the year.

Freedom of Information
Experts were reminded that any FOI queries that they receive from the media were to be referred to the Secretariat.

Membership
Members were asked to let the Secretariat know if any of their details had changed.

415 **General Matters** **ABS(18)32**

Fire evacuation procedure
Members were introduced to the new evacuation procedure in the event of a fire alarm.

MINUTES **ABS(18)33**

416 The minutes and summary minutes of the meeting held on 27th February 2018 were confirmed.

II **MATTERS ARISING FROM THE MINUTES** **ABS(18)34**

417 The following matters arising from the meeting held on 27th February 2018 were noted.

Teicoplanin Injection (minute 385 refers) The draft new monograph would be included in a future BP publication, subject to comments from manufacturers

Lymecycline Capsules (minute 385 refers) A draft monograph would be included in a future publication

Tylosin Premix (minute 385 refers) The draft monograph would be included in a future publication..

Doxycycline Preparations (minute 388 refers) The monographs were published in the BP 2019.

Doxorubicin Preparations (minute 389 refers) The monographs were published in the BP 2019.

Moxidectin Preparations (minute 390 refers) The monographs were published in the BP 2019.

Norfloxacin Tablets (minute 391 refers) The monographs were published in the BP 2019.

Tigecycline for Infusion (minute 392 refers) The monographs were published in the BP 2019.

Benzylpenicillin Injection (minute 393 refers) A monograph would be included in a future publication.

Phenoxymethylpenicillin preparations (minute 394 refers) The monographs would be included in a future publication.

Clindamycin Preparations (minute 395 refers) The monographs would be included in a future publication.

Minocycline Preparations (minute 396 refers) The monographs were intended to be published in the BP 2020.

Caspofungin for Injection (minute 397 refers) A monograph would be included in a future publication.

Ciclosporin Preparations (minute 398 refers) The monographs would be included in a future publication.

Rifampicin Combination Preparations (minute 403 refers) The draft new monograph would be included in a future BP publication, subject to comments from manufacturers

III MONOGRAPHS FOR THE BP 2020

418 Phenoxymethylpenicillin Preparations **ABS(18)52**
Phenoxymethylpenicillin Tablets
Phenoxymethylpenicillin Oral Solution

A revision to the Phenoxymethylpenicillin Potassium Ph. Eur. monograph had been published, which included an improved HPLC method for Related substances and Assay. The Secretariat presented draft monographs and a laboratory plan to incorporate these changes into the BP product monographs at the February 2018 meeting of the EAG. Laboratory work on this project had been agreed and was in progress.

Tablets Monograph
The work on the Tablets monograph for Related substances and Assay had been completed successfully and a report prepared.

Oral Solution
Members were updated with the progress of the revision of the monograph.

Members agreed that the method was suitable for inclusion in the monograph on the basis that the Secretariat work with the Laboratory to provide sufficient disregard instructions. The revised monograph would be presented at a future meeting of the EAG.

419 Azithromycin Eye Drops ABS(18)35

The draft new monograph would be included in a future BP publication, subject to comments from manufacturers.

420 Cilastatin and Imipenem for Infusion ABS(18)36

The draft new monograph would be included in a future BP publication, subject to comments from manufacturers

421 Co-amoxiclav Injection ABS(18)37

Following recent queries from stakeholders regarding the Co-amoxiclav Injection monograph, it was highlighted that a BPCRS used in the monograph was out of stock (Amoxicillin Impurity Standard BPCRS). The Secretariat noted that the BPCRS had high usage among stakeholders and so would be beneficial to users to have back in stock.

Members agreed that the re-establishment of the BPCRS was vital to the compliance of the monograph and was important to the in-stock levels of the BPCRS library. The Secretariat proposed that Impurity J be removed from the BPCRS mixture and that impurity J be identified through relative retention in the monograph.

422 Colistimethate Inhalation Powder, Hard Capsule ABS(18)38

The draft new monograph would be included in a future BP publication, subject to comments from manufacturers

423 Colistin Tablets ABS(18)39

The revision of the Colistin Tablets monograph had been on the ABS work programme for some time, however the Ph. Eur. had recently updated the Colistin Sulfate monograph in Supplement 9.6. This update incorporated the modernisation of the monograph, consisting of the revision of the Composition test as well as an update to the limits for impurities in the Related substances test to align with ICH and current safety guidelines.

It was highlighted that there were no manufacturers of Colistin Tablets in the UK, however there was a usage of 13 prescriptions.

Proposal
The Secretariat proposed that the monograph should be updated and further assigned to the Unlicensed Medicines EAG (ULM). The expertise in this group would ensure that the monograph would be most suitable for the unlicensed use of Colistin Tablets. The

transfer of the monograph would rely on the confirmation that Colistin Tablets are no longer under license in the UK.

424 **Erythromycin Preparations** **ABS(18)40**
Gastro-resistant Erythromycin Capsules
Gastro-resistant Erythromycin Tablets
Erythromycin Lactobionate Infusion
Erythromycin and Zinc Acetate Lotion
Erythromycin Ethylsuccinate Tablets
Erythromycin Ethylsuccinate Oral Suspension
Erythromycin Stearate Tablets

Laboratory work for the Erythromycin family of monographs had been in progress for a while, the Secretariat provided an update to the project along with the presentation of the finalised laboratory report for Erythromycin Lactobionate for Infusion.

Dissolution
The dissolution test for the Gastro-resistant capsules had been found to be unsuitable. A separate dissolution medium had been sought, which used the Assay HPLC method for quantitative analysis. Laboratory work was ongoing.

Erythromycin Lactobionate for Infusion
A draft monograph and laboratory report for Erythromycin Lactobionate for Infusion were presented to the EAG. Members requested that manufacturers be contacted to confirm the suitability of impurity limits during public consultation.

Members discussed that registered specifications had controls for “free lactobionic acid” however, members agreed that the pH limits in the monograph would be adequate control for the drug product.

425 **Griseofulvin Preparations** **ABS(18)41**
Griseofulvin Premix
Griseofulvin Tablets

A revision to the Griseofulvin Tablets monograph was first discussed at the September 2017 meeting of the EAG. Draft revised monographs for Griseofulvin Tablets and Griseofulvin Premix were presented to the EAG.

Identification
Members discussed the removal of the Colour and UV tests from the monograph as it was deemed that the IR procedure was discriminatory enough to be used as a sole identification tool.

Related substances
The method for Related substances had been drafted from the Ph. Eur. Related substances method for Griseofulvin. Impurity limits were harmonised with the drug substance with the exception of the unspecified impurities and limit of disregard which were in-line with VICH GL11 and ICH Q3B(R2) for the Premix and Tablets monographs respectively.

Members requested that the licensed manufacturers be contacted when the draft monographs were on the website.

Assay
A HPLC procedure harmonised with the Related substances was included in the draft monographs for analytical convenience.

Members agreed on the inclusion of the method for Assay as it replaced a less specific UV absorbance test.

426 **Tobramycin Preparations** **ABS(18)42**
Tobramycin Eye Drops
Tobramycin Inhalation Powder, Hard Capsule
Tobramycin and Dexamethasone Eye Drops

The draft new monographs would be included in a future BP publication, subject to comments from manufacturers

MONOGRAPHS FOR THE BP 2021

427 **Vancomycin Preparations** **ABS(18)43**
Vancomycin Oral Solution
Vancomycin Infusion
Vancomycin Capsules
Vancomycin Eye Drops

Revisions to the Vancomycin Product monographs were presented to the EAG. Members noted that it may be beneficial to assess this procedure for the unlicensed Vancomycin Eye Drops monograph as part of a family of monographs and agreed that EAG ULM should be consulted.

Related substances and Vancomycin B
A new method with the ability to determine the level of Vancomycin B and its Related substances had been published by the Ph. Eur which provided greater control of impurities.

Members discussed the limits for the Infusion and Oral Solution products, which had been based on limits in the EP, manufacturers current specifications and ICH guidelines for fermentation products. Members agreed that the limits for the Capsules monograph would be reviewed following laboratory assessment.

MONOGRAPHS FOR THE BP 2022+

428 **Chloramphenicol Preparations** **ABS(18)44**
Chloramphenicol Capsules
Chloramphenicol Ear Drops
Chloramphenicol Eye Drops
Chloramphenicol Eye Ointment

The Ph. Eur. had recently updated the Chloramphenicol API monograph which incorporated improved Related substances and Assay procedures. The draft revised monographs were presented to the EAG.

Identification
The identification tests in the published Chloramphenicol product monographs required extraction through the use of Petroleum Spirit and ether. An IR method had been sought for the draft monographs to ensure that these chemicals were no longer required. Members discussed the procedures and requested that suitable extraction procedures would need to be investigated prior to publication.

Dissolution (Capsules only)
Members discussed revised limits in the draft monograph and agreed that the

Laboratory investigate the dissolution of Chloramphenicol Capsules that are currently on the market.

Related substances
A new Related substances procedure for chloramphenicol had been recently adopted by Ph Eur. The method had been drafted into the chloramphenicol family monographs. Members discussed the draft limits and proposed that a review of the limits would be performed after a laboratory assessment of the products.

Assay
Members discussed the draft Assay method that had been harmonised with the drafted Related substances procedure and agreed that the laboratory performed an assessment of the method with the Chloramphenicol products.

FOR INFORMATION

429 Benzoyl Peroxide and Clindamycin Gel ABS(18)45

A laboratory report confirming dichloromethane as a suitable replacement for chloroform in the identification test was presented for members information.

430 Review Of The Use Of Antimicrobial Assays ABS(18)46

The Secretariat presented a paper detailing the BPs current position on the use of Antimicrobial Assays including historical reviews and usage data in current monographs. The paper highlighted the complexity and difficulties in replacing antimicrobial Assays with chemical analysis and referred to a World Health Organisation initiative to characterise an international Primary standard for Capreomycin Sulfate for a Chemical Assay.

Members agreed to ascertain the appetite for change to chemical Assays within their networks and investigate how this could be undertaken.

431 Review of out of stock BPCRS for EAG ABS ABS(18)47

The Secretariat had undertaken a review of out of stock BPCRS related to ABS monographs. Members agreed that the Ceftriaxone Injection monograph should utilised Ceftriaxone Impurity A EPCRS instead of the BPCRS equivalent.

432 Work Programme ABS(18)48

The ABS work programme was presented to members for information.

Members endorsed the addition of the following monographs to the BP work programme:

Piperacillin and Tazobactam Injection/infusion
Doxycycline Oral Suspension
Ritonavir Tablets
Ritonavir Powder Sachet
Clindamycin Oral Suspension
Clindamycin Oral Solution
Cefalexin Granules for Syrup.

Due to a lack of use in the following products, members agreed to remove them from the work programme, subject to agreement from BPC and the VMD:

Danofloxacin Injection
Amphotericin Irrigation Solution
Amphotericin Concentrate
Moxidectin Pour on solution

433 British Pharmacopoeia Matters ABS(18)49

A summary of the minutes from the latest BPC meeting was presented for information.

434 Use Of Fish Peptone In Manufacture Of Antibiotics ABS(18)50

Mr Sumal presented a short update regarding an ongoing issue with the use of fish peptones in the fermentation process of the manufacture of certain antibiotics.

435 European Pharmacopoeia ABS(18)51

An update on changes to Ph. Eur. monographs that affected ABS monographs was presented to members.

436 Any Other Business

None.

437 Date of Next Meeting

7th February 2019.